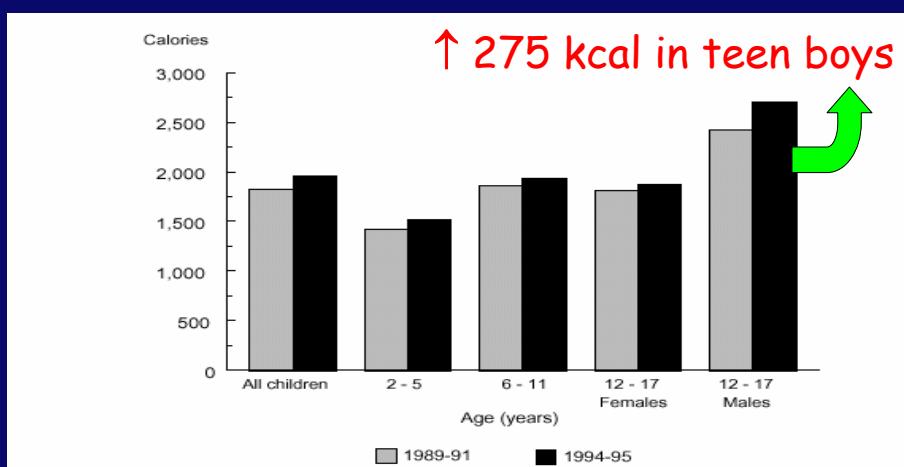


What happened to willpower? I love fat people. Every fat person says it's not their fault, that they have gland trouble. You know which gland? The saliva gland. They can't push away from the table.

Jesse Ventura (I), Former Governor of Minnesota. *Playboy*, November 1999;46:55.

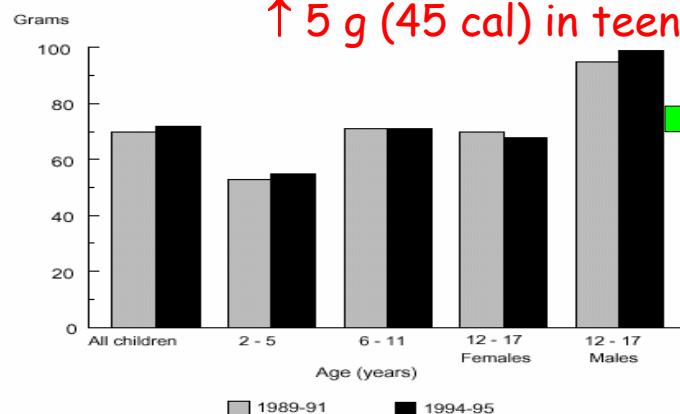
Total Caloric Intake



Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95
<http://www.usda.gov/cnpp/FENR%20V11N3/fenrv11n3p44.PDF>

Fat Intake: Grams

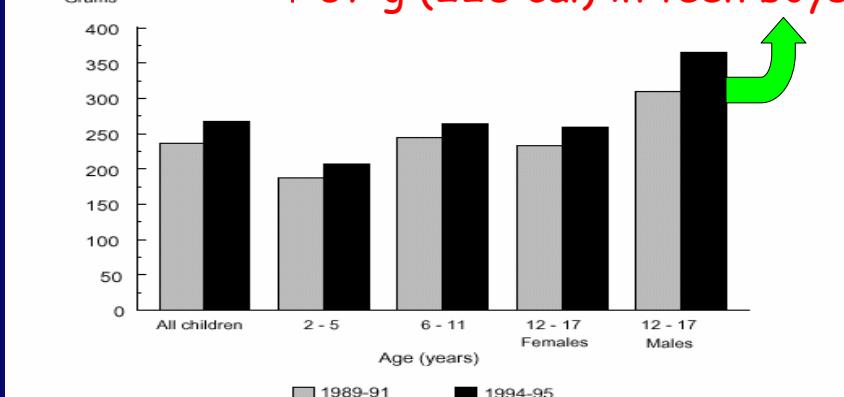
↑ 5 g (45 cal) in teen boys



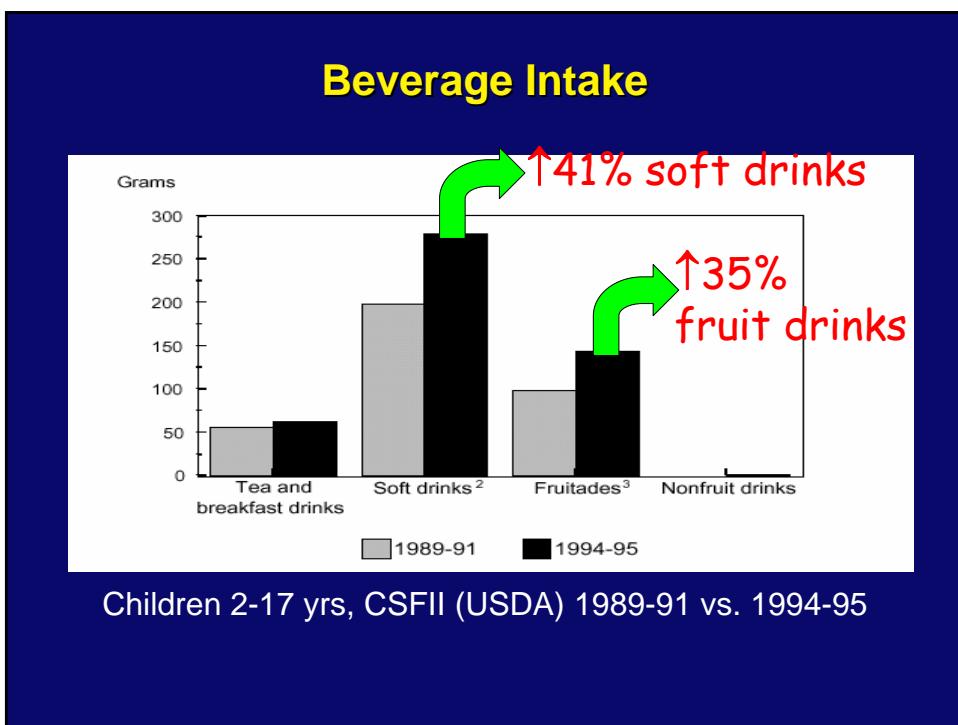
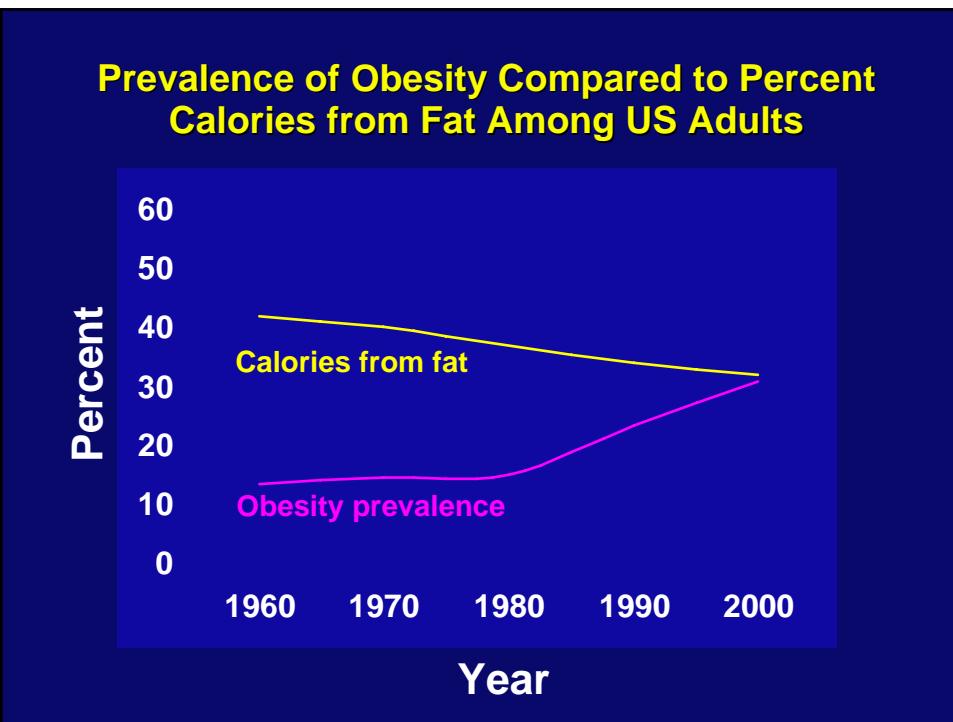
Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

Carbohydrate Intake: Grams

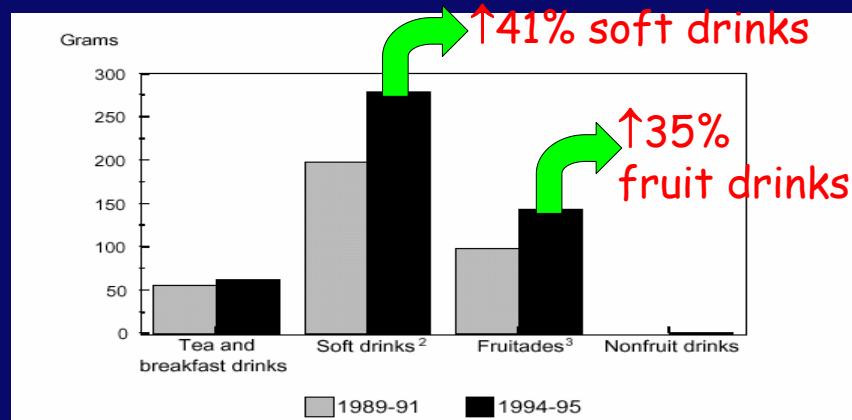
↑ 57 g (228 cal) in teen boys



Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95



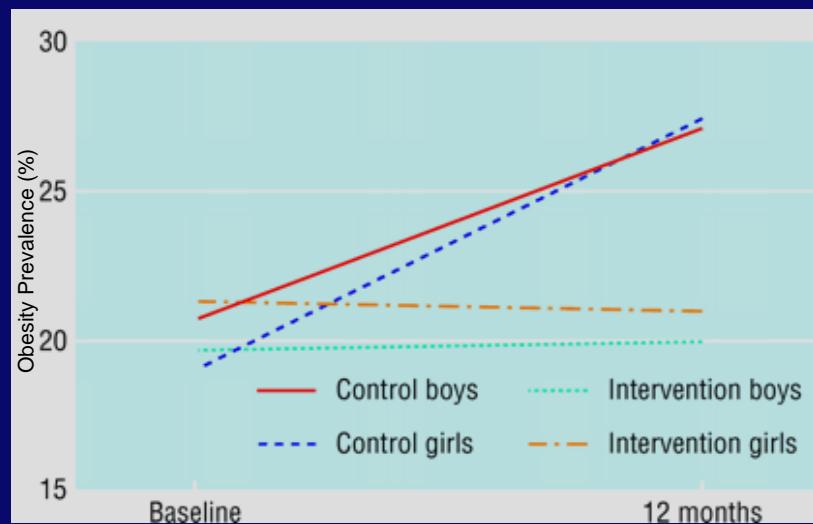
Beverage Intake



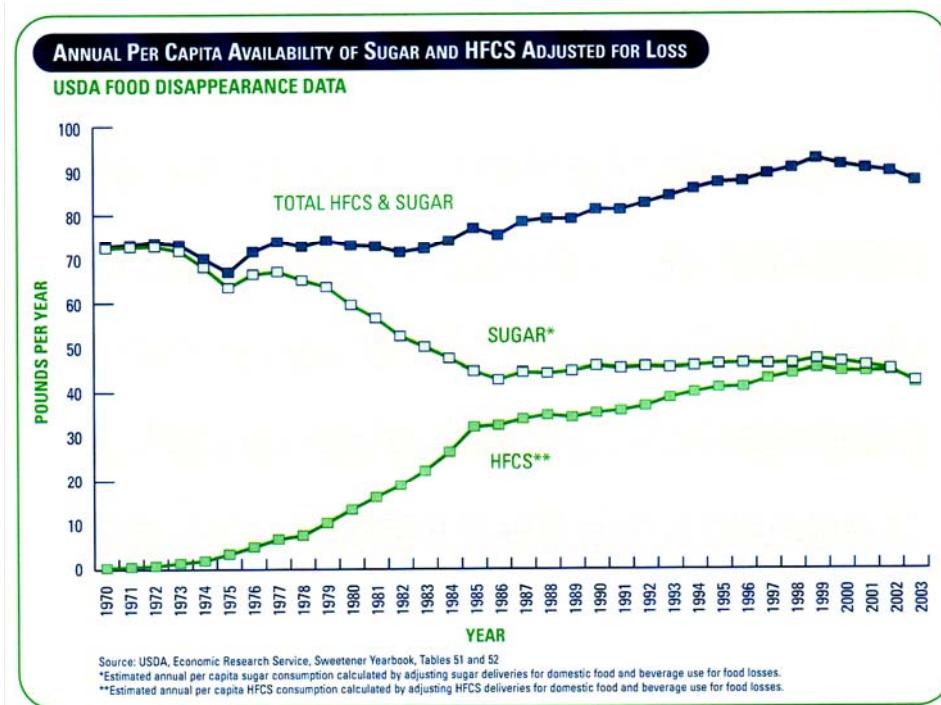
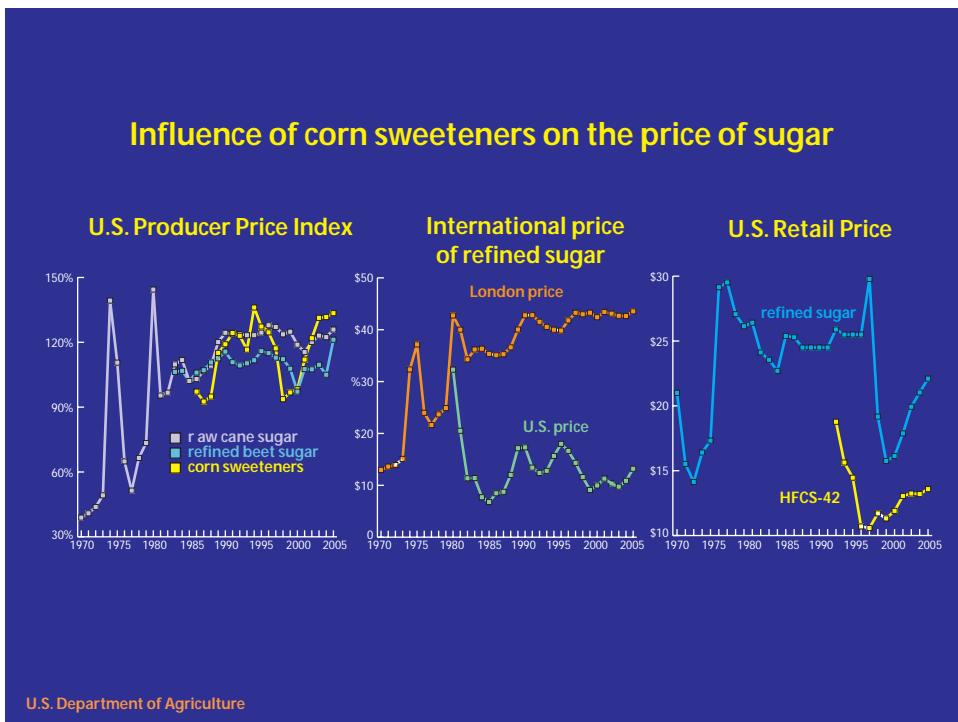
Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

One can of soda/day = 150 cal x 365 d/yr ÷ 3500 cal/lb = 15.6 lbs/yr!

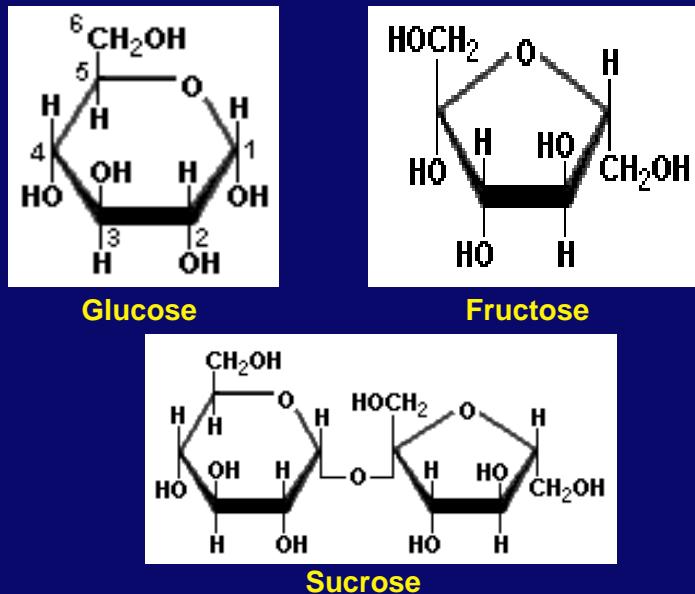
Curtailing soft drinks limits childhood obesity



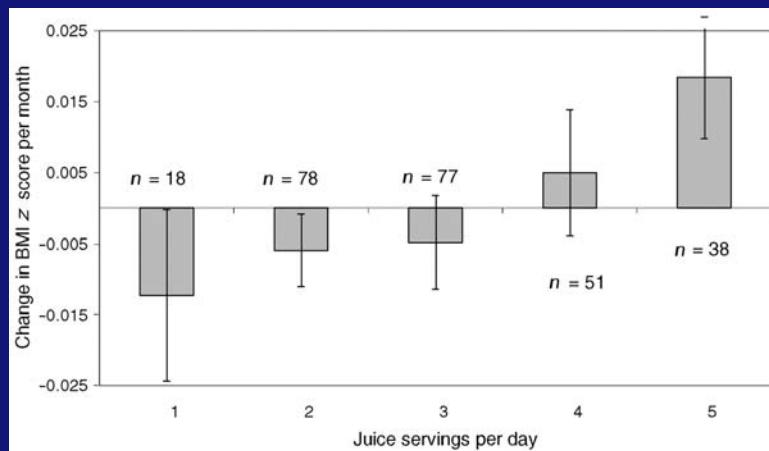
James et al. BMJ 328:1237, 2004



**High Fructose Corn Syrup is 42-55% Fructose;
Sucrose is 50% Fructose**



**Juice is sucrose:
Change in BMI z-score in lower socioeconomic status
children versus number of fruit juice servings per day**



Faith MS et al. Pediatrics 118:2066, 2006

Fructose is not glucose

- Fructose is 7 times more likely than glucose to form Advanced Glycation End-Products (AGE's)
- Fructose does not suppress ghrelin
- Acute fructose does not stimulate insulin (or leptin)
- Hepatic fructose metabolism is different
- Chronic fructose exposure promotes the Metabolic Syndrome

Elliot et al. Am J Clin Nutr, 2002
Bray et al. Am J Clin Nutr, 2004
Teff et al. J Clin Endocrinol Metab, 2004

Gaby, Alt Med Rev, 2005
Le and Tappy, Curr Opin Clin Nutr Metab Care, 2006
Wei et al. J Nutr Biochem, 2006

Ethanol is a carbohydrate

Ethanol is a carbohydrate



Ethanol is a carbohydrate



But ethanol is also a toxin

Acute ethanol exposure

- CNS depression
- Vasodilatation, decreased BP
- Hypothermia
- Tachycardia
- Myocardial depression
- Variable pupillary responses
- Respiratory depression
- Diuresis
- Hypoglycemia
- Loss of fine motor control

Acute fructose exposure

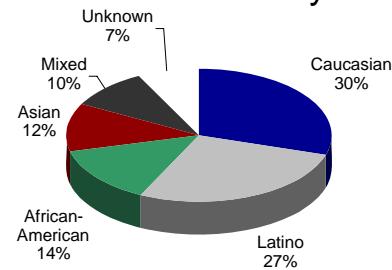
UCSF Weight Assessment for Teen and Child Health (WATCH) Clinic

294 patients 2003-2006

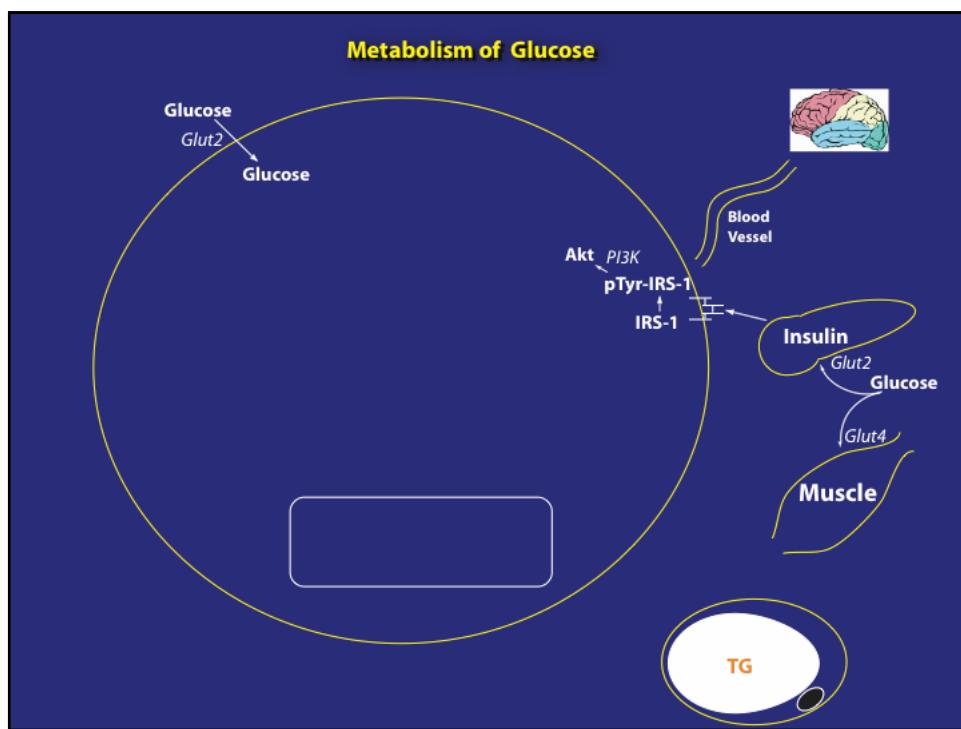
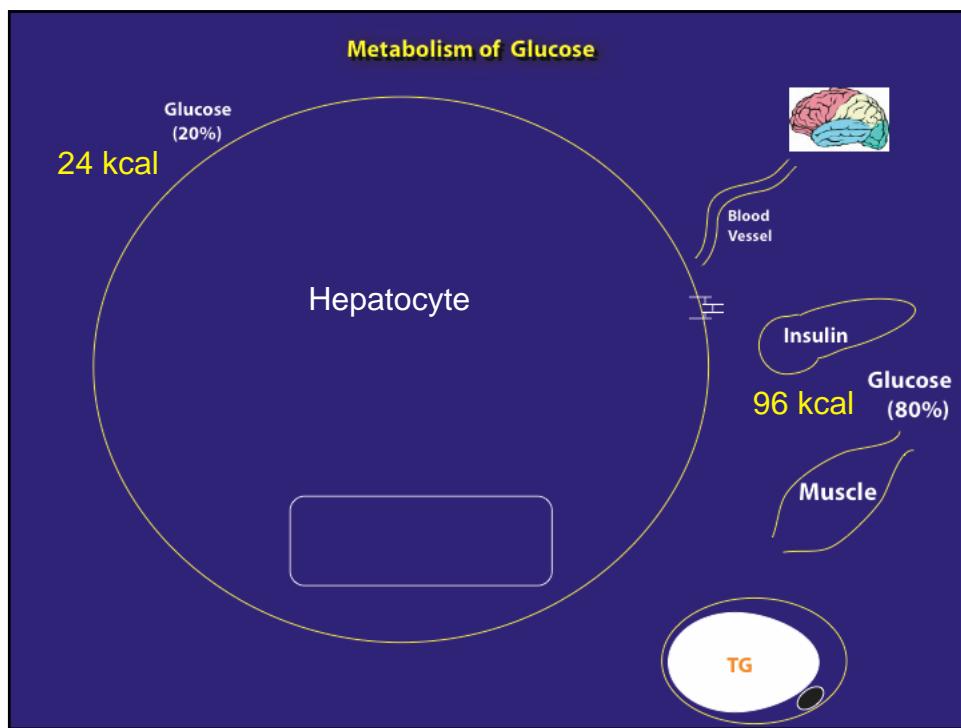
• Biochemistry

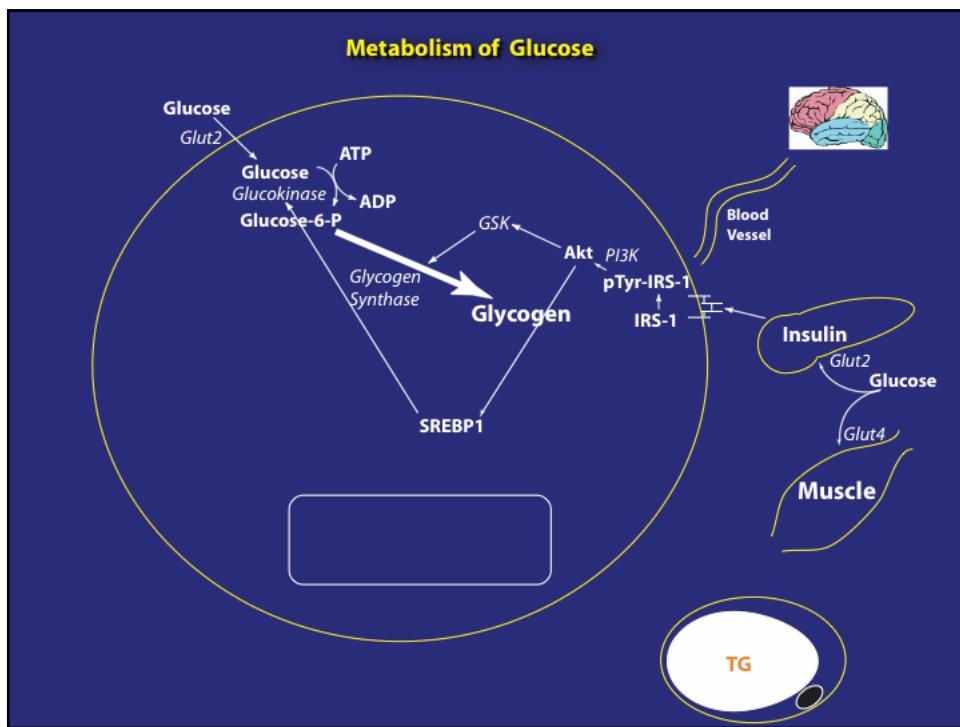
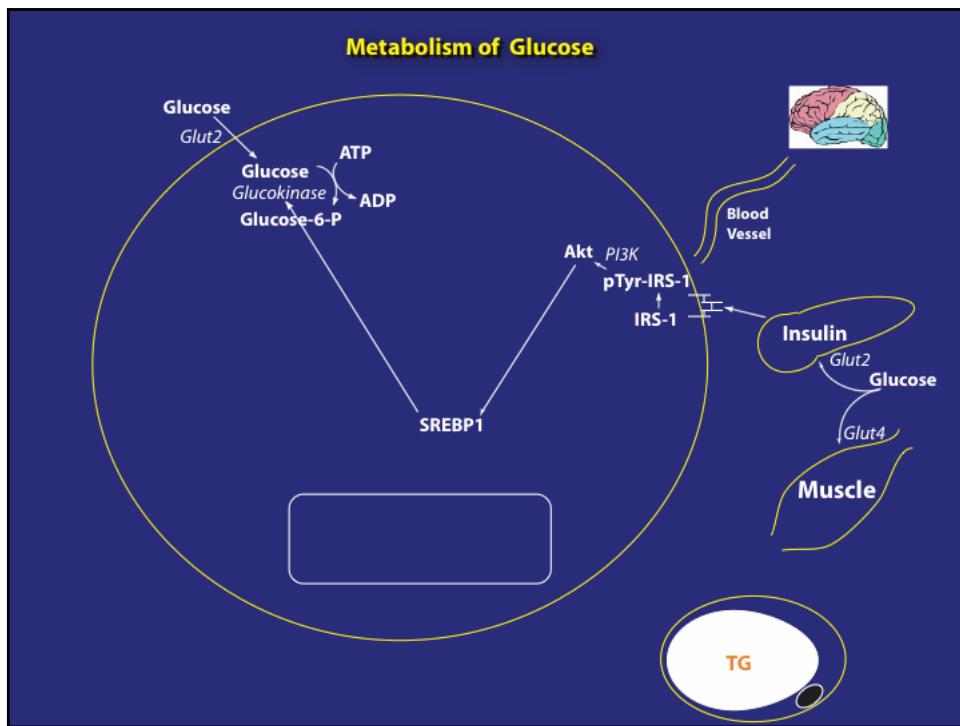
	Median	Min	Max	Normal
BMI	33.2	20.0	92.4	<25
BMI z-score	2.5	1.3	4.4	0
FBG	87	58	119	<100
Insulin	20.7	2	117.5	5-20
HOMA-IR	4.3	0.34	28.1	<4
Maternal BMI	28.9	17.7	58.6	<25
Paternal BMI	28.9	16.7	48.8	<25

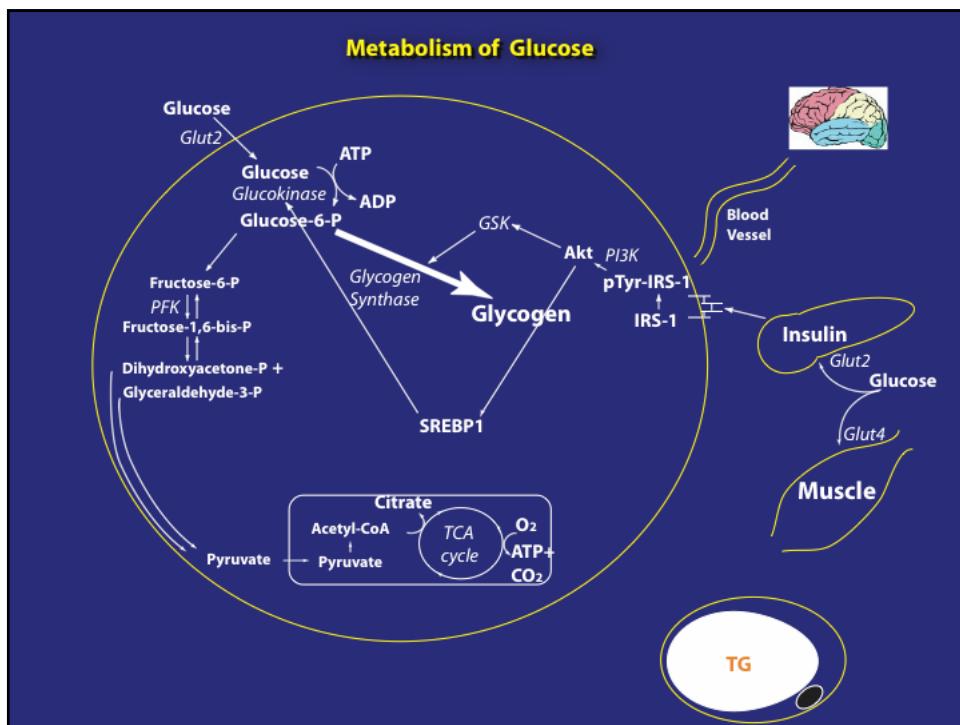
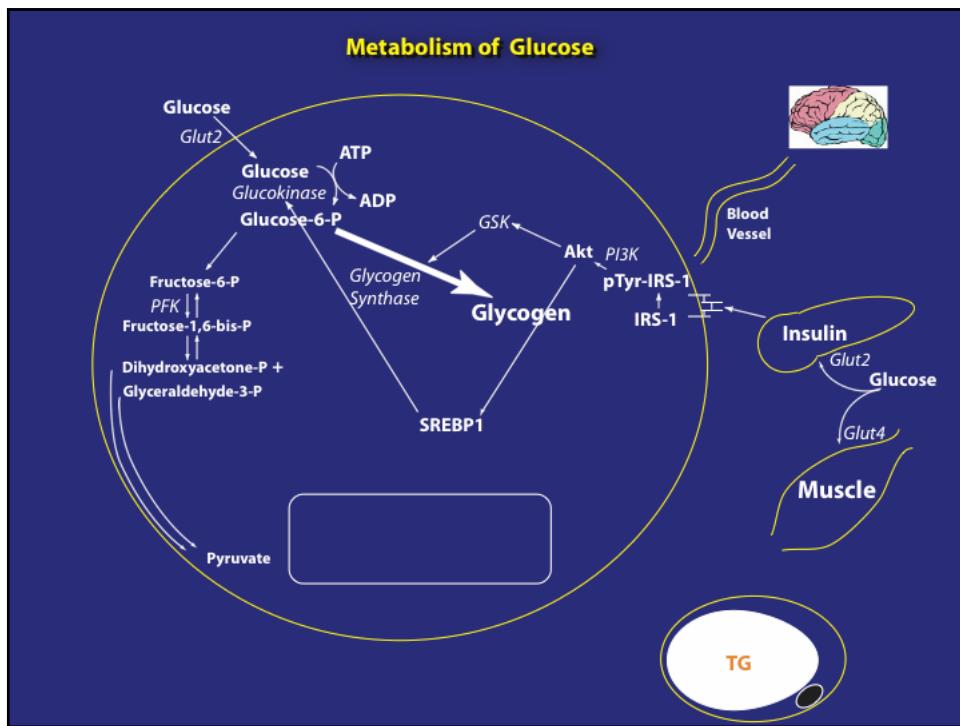
• Race/Ethnicity

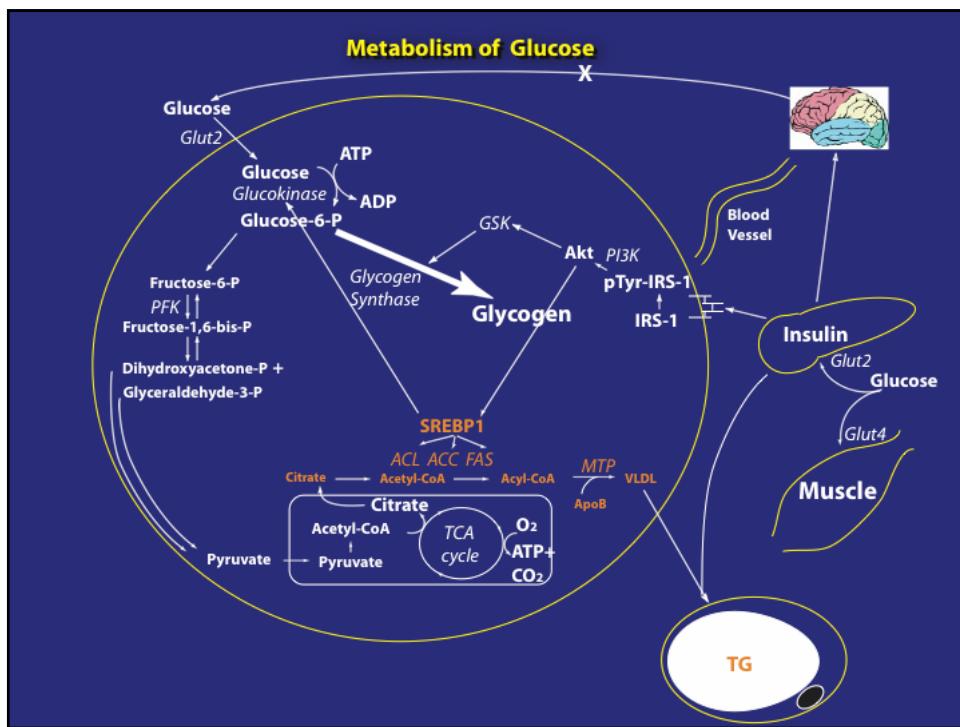
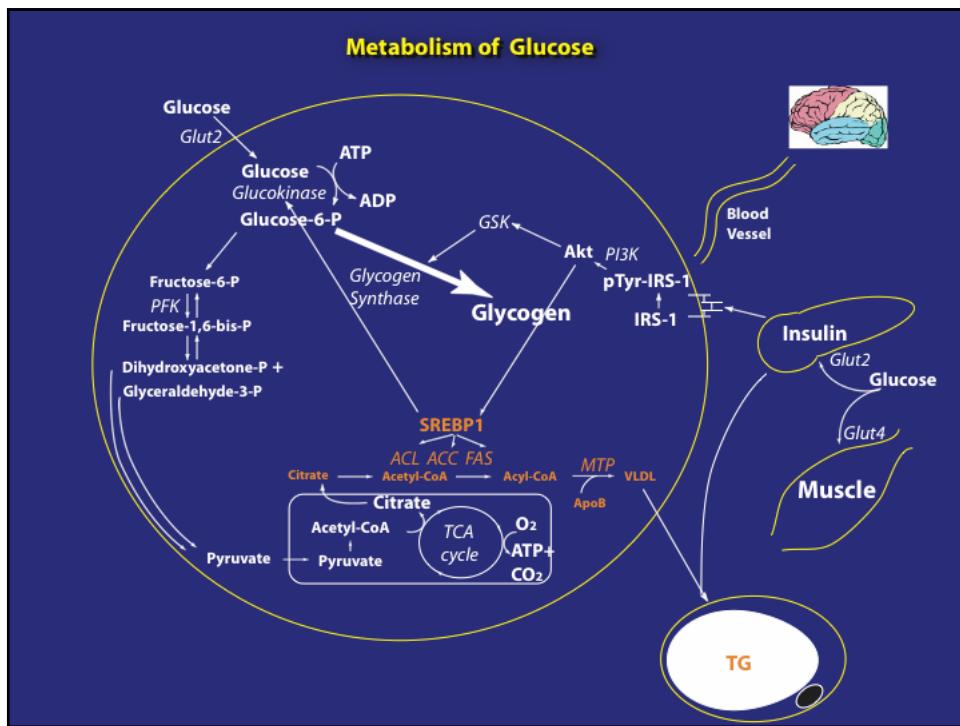


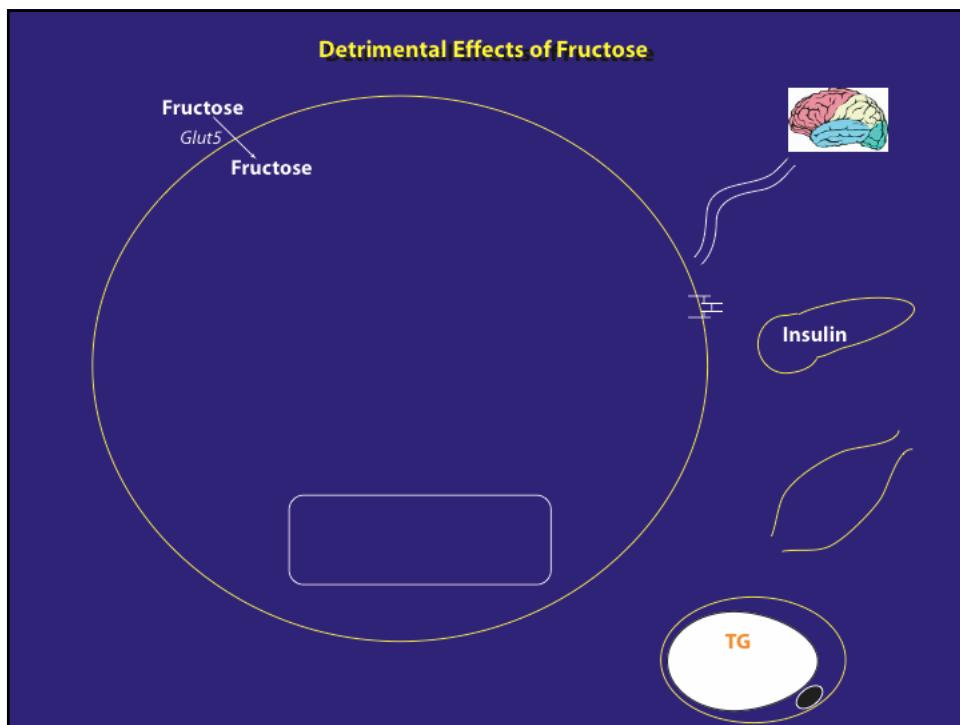
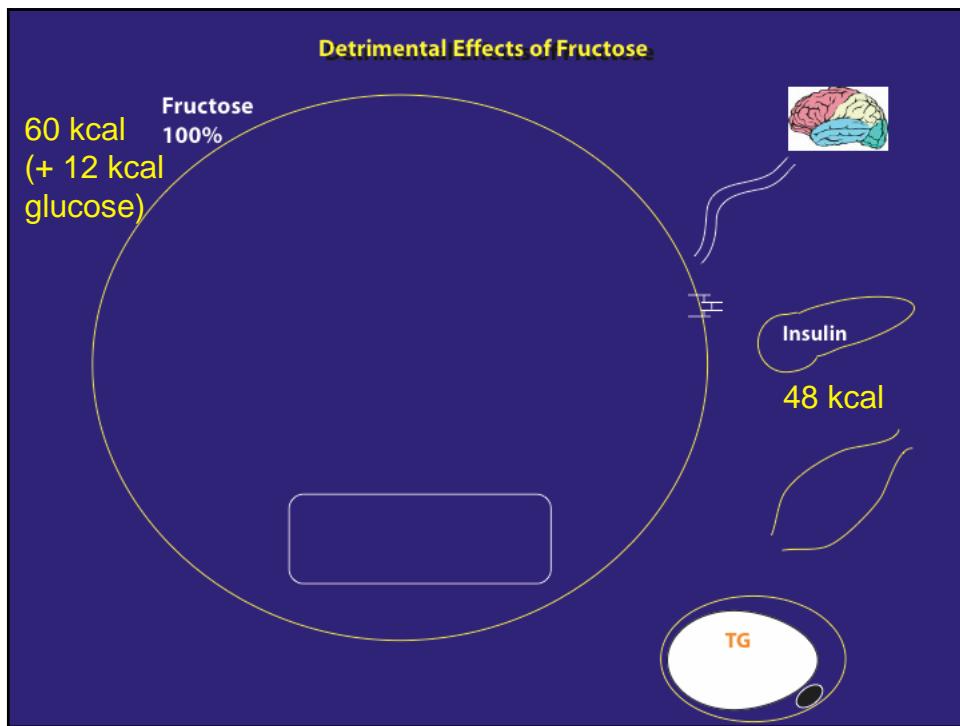
Mietus-Snyder et al. (submitted)

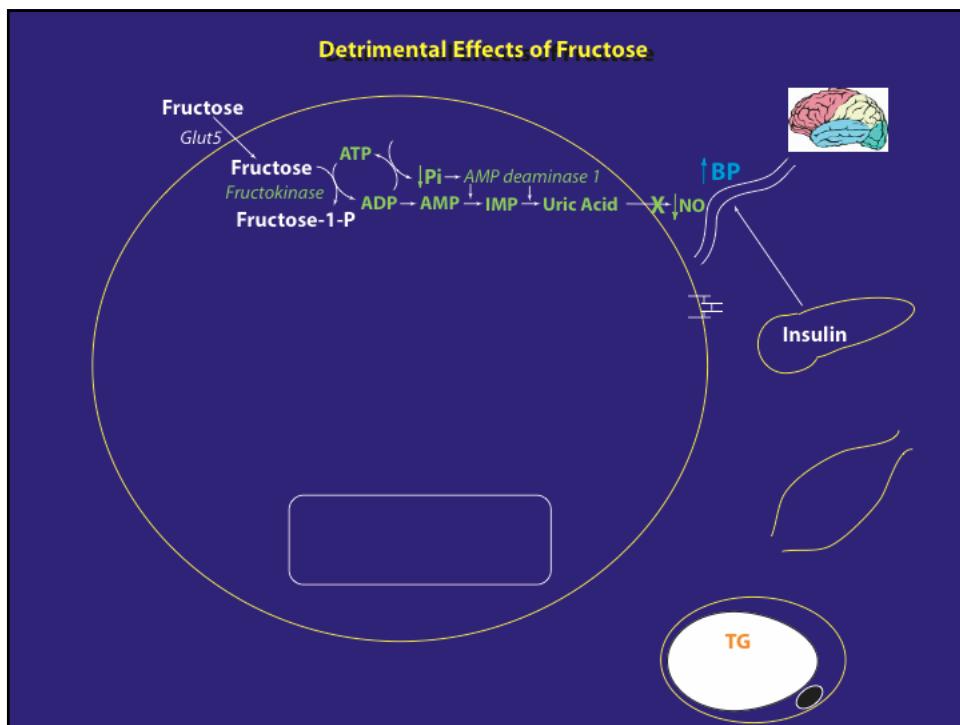
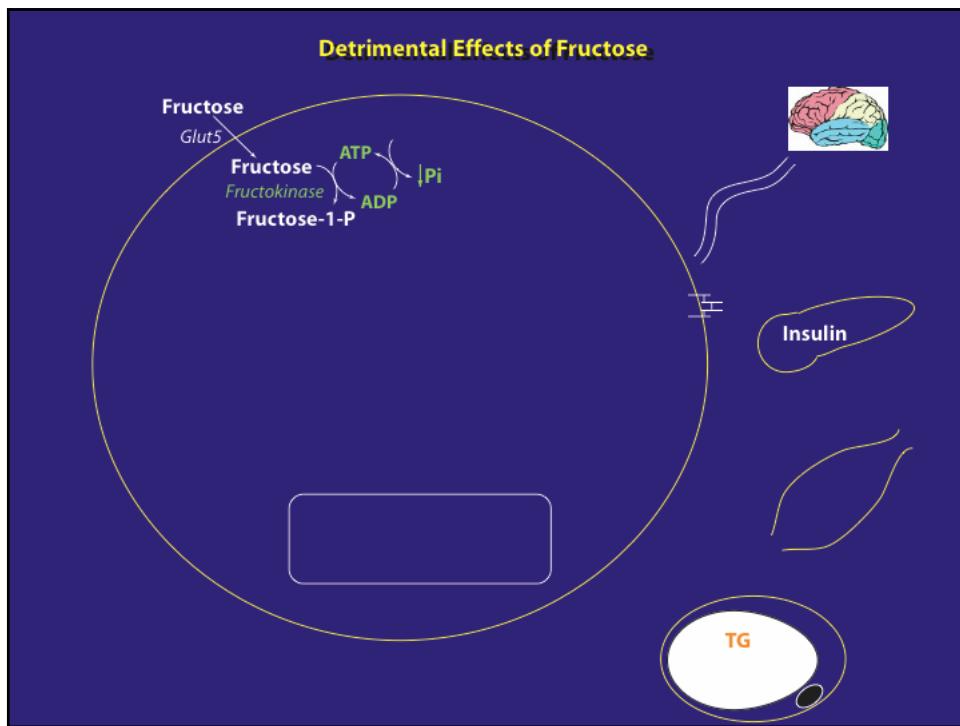




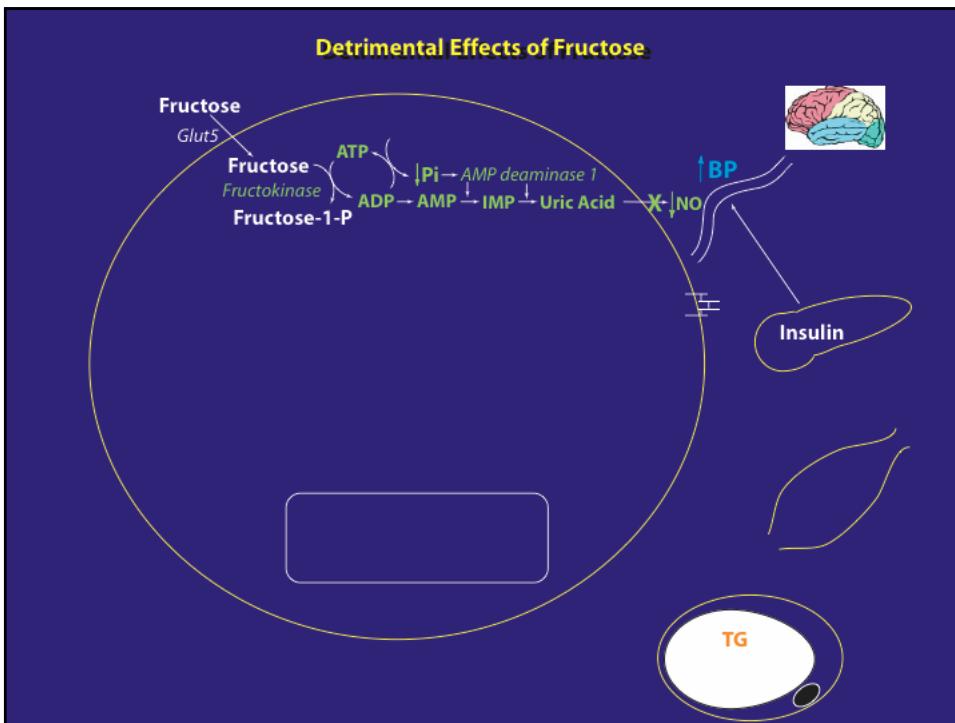
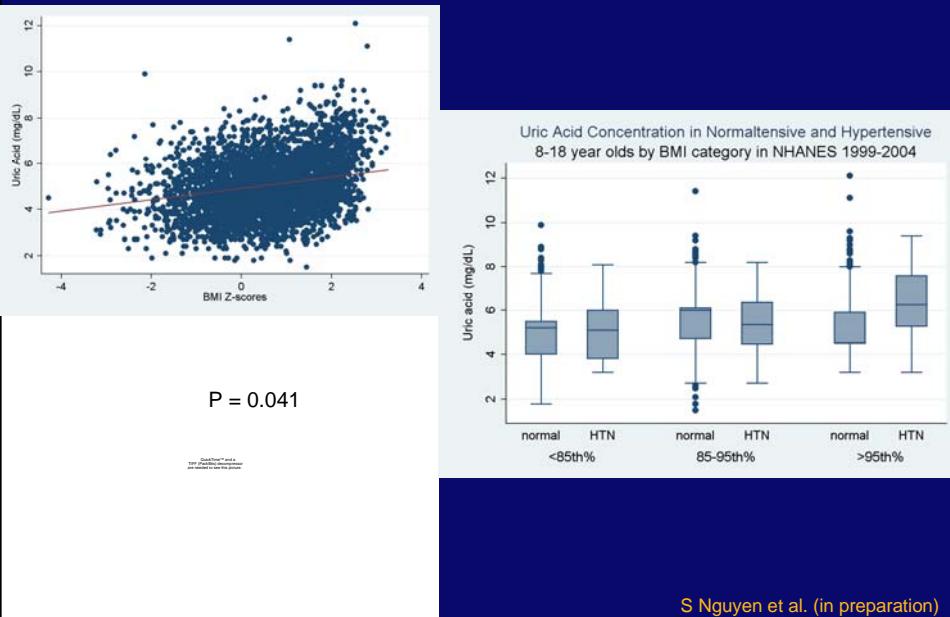


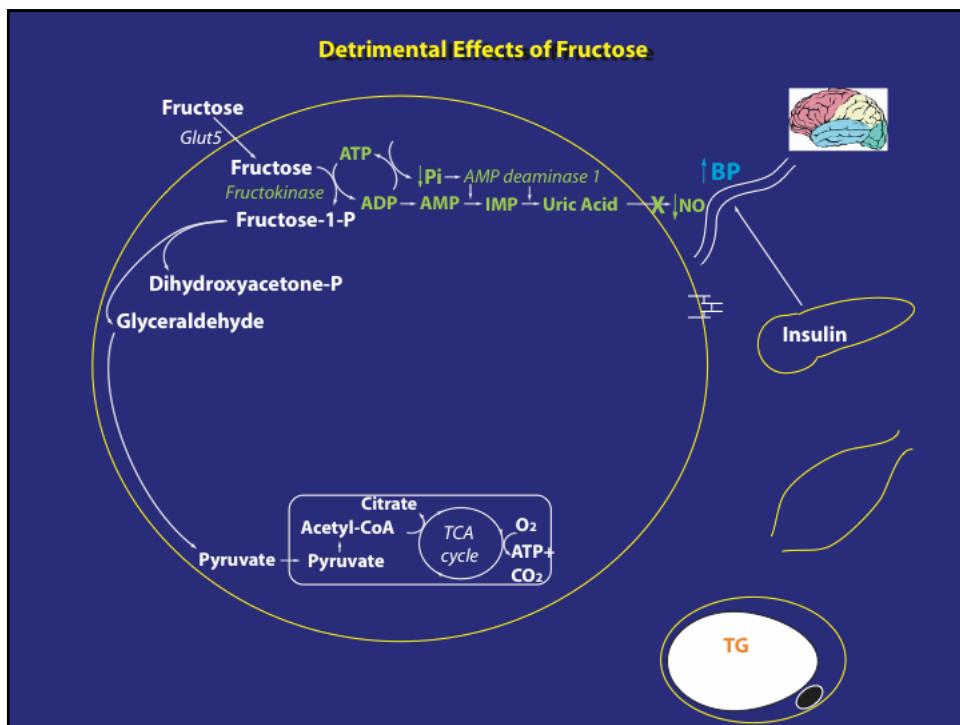
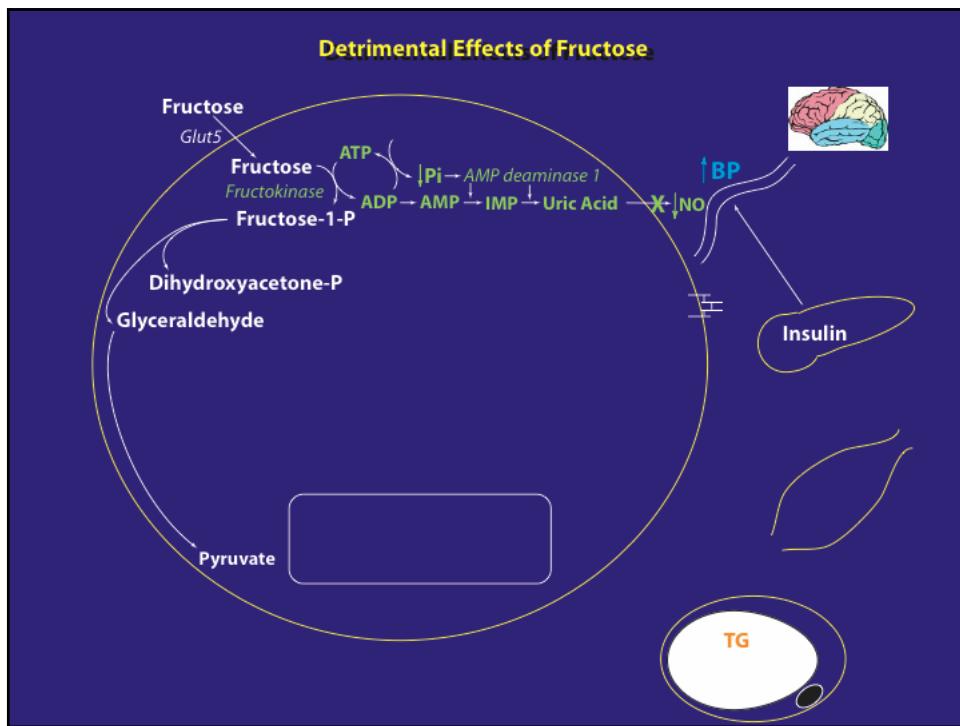


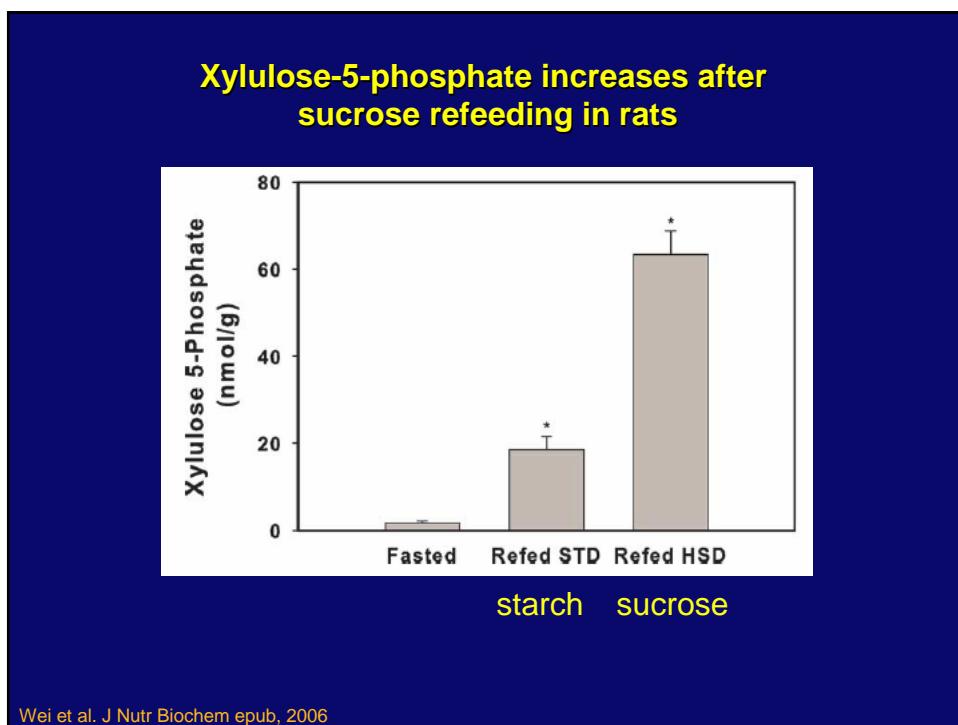
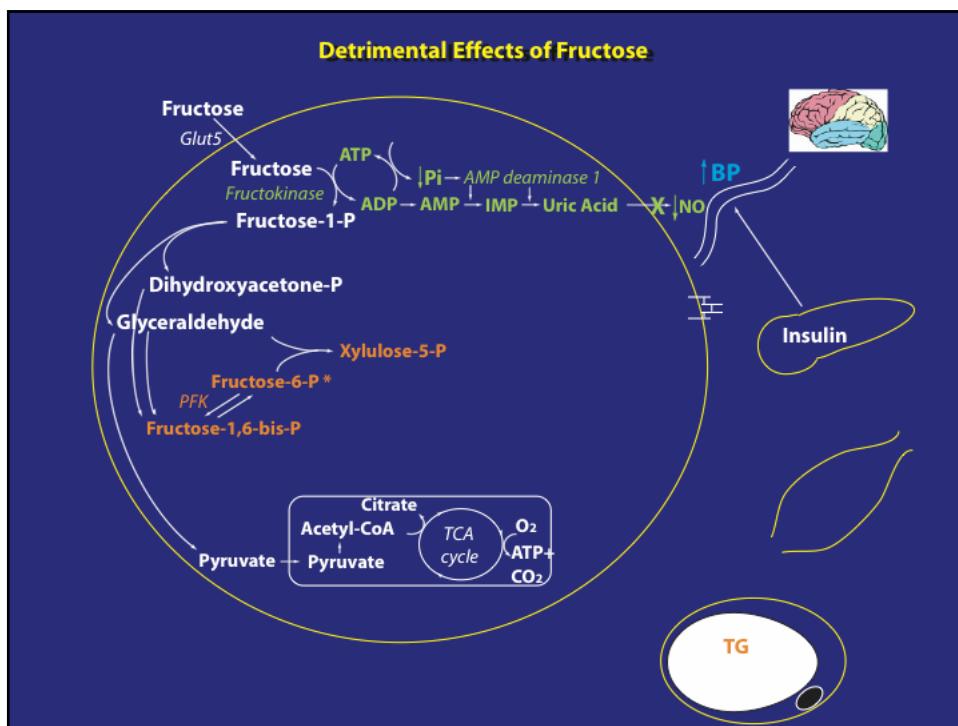


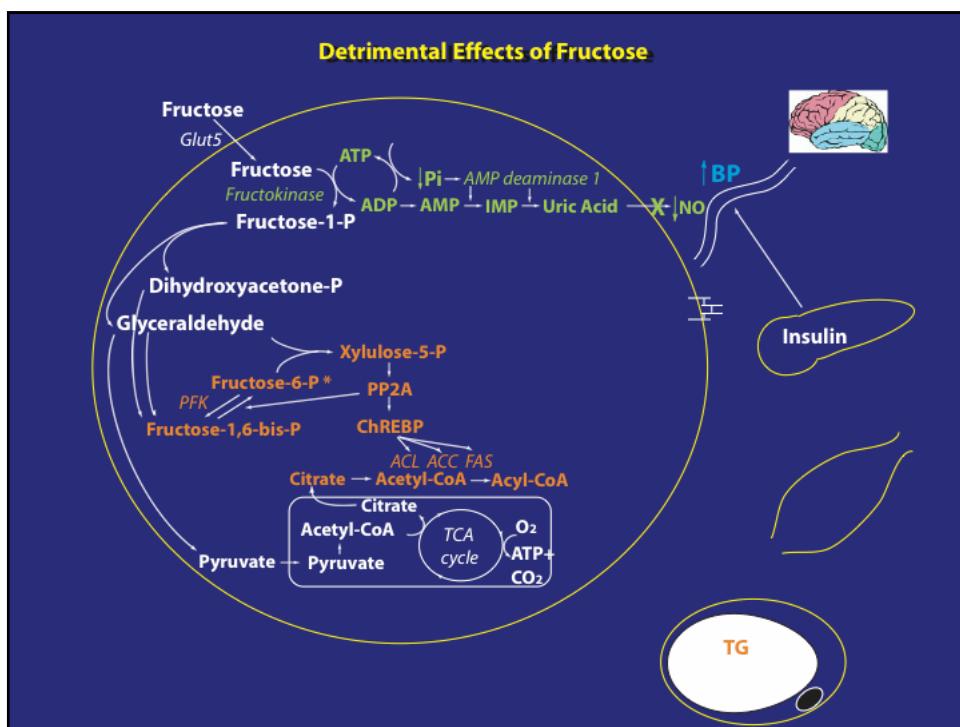
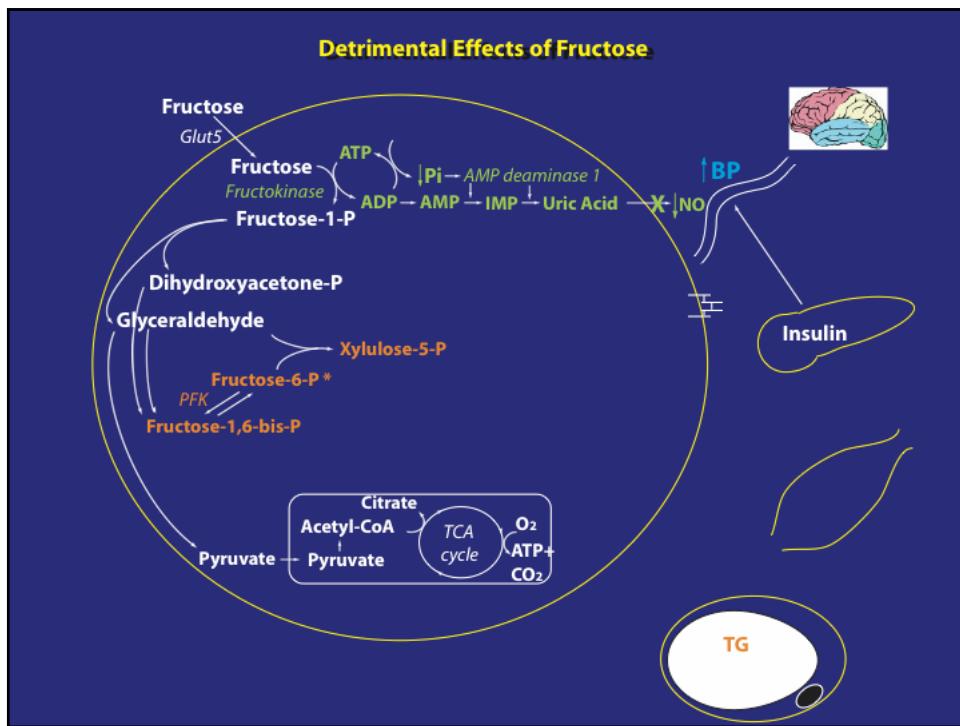


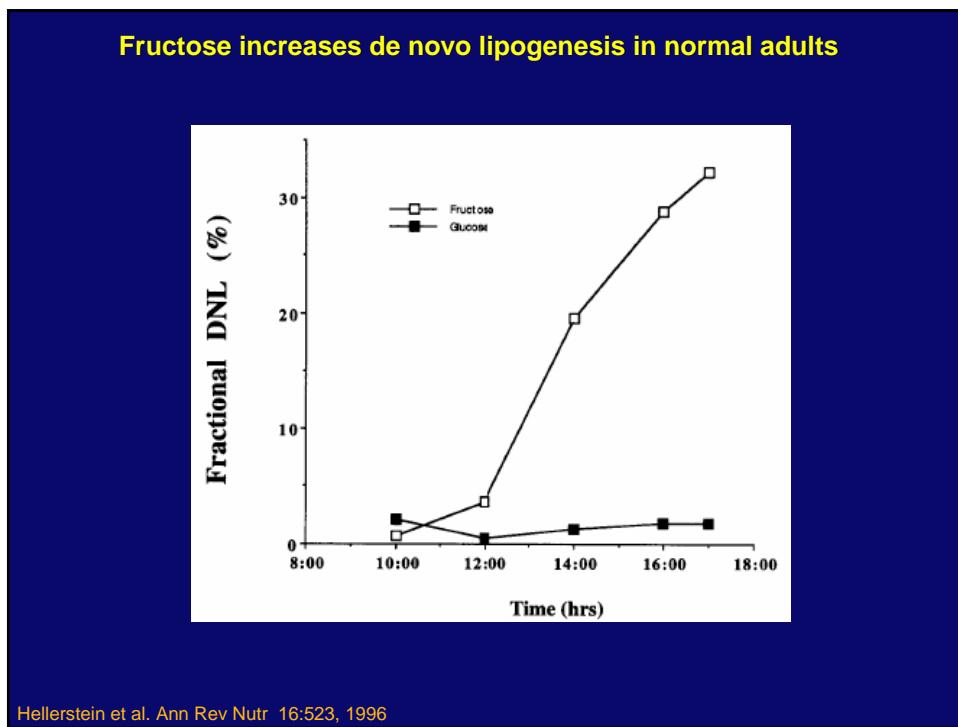
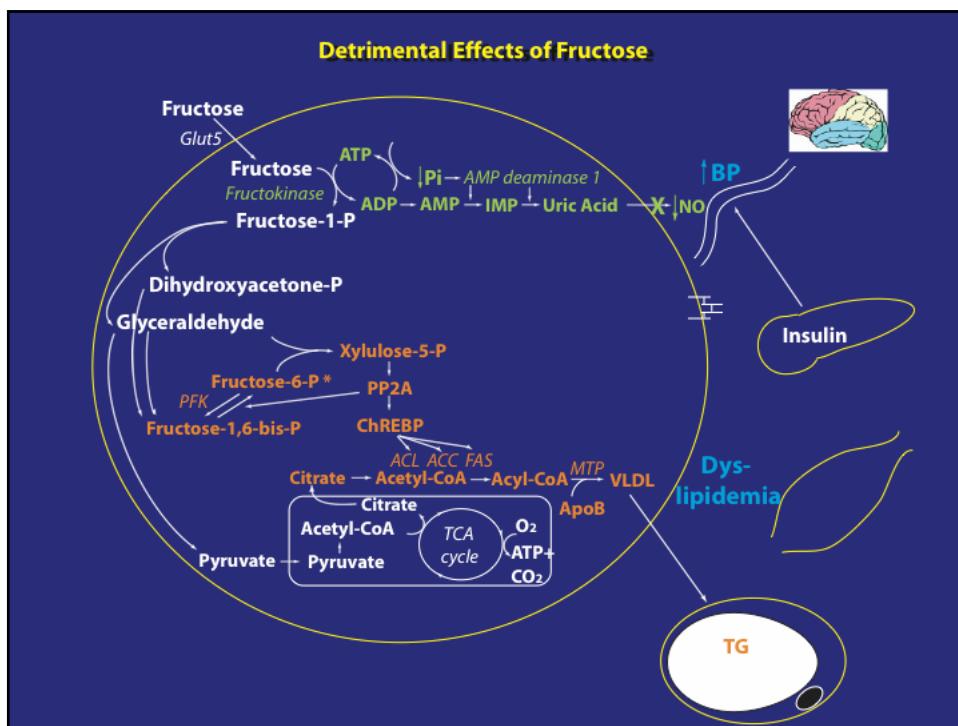
Relations between uric acid, hypertension, obesity, and fructose in NHANES IV children











Fructose increases de novo lipogenesis, triglycerides and free fatty acids in normal adults

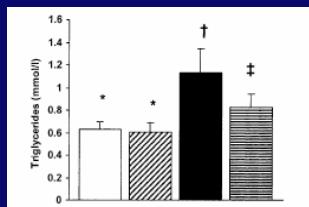


FIG. 3. Mean fasting triglyceride concentration after control condition (□), after 28 days of fish oil supplementation (▨), after 6 days of high-fructose diet (■), and after 28 days of fish oil supplementation plus high-fructose diet (▨) in seven men. Values are means \pm SE represented by vertical bars. *Values not sharing the same superscript are significantly different ($P < 0.05$).

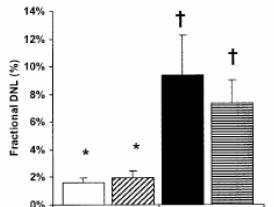


FIG. 4. Mean baseline fractional hepatic DNL after control condition (□), after 28 days of fish oil supplementation (▨), after 6 days of high-fructose diet (■), and after 28 days of fish oil supplementation plus high-fructose diet (▨) in seven men. Values are means \pm SE represented by vertical bars. *Values not sharing the same superscript are significantly different ($P < 0.05$).

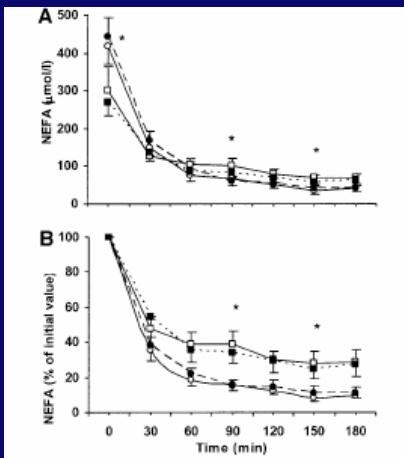
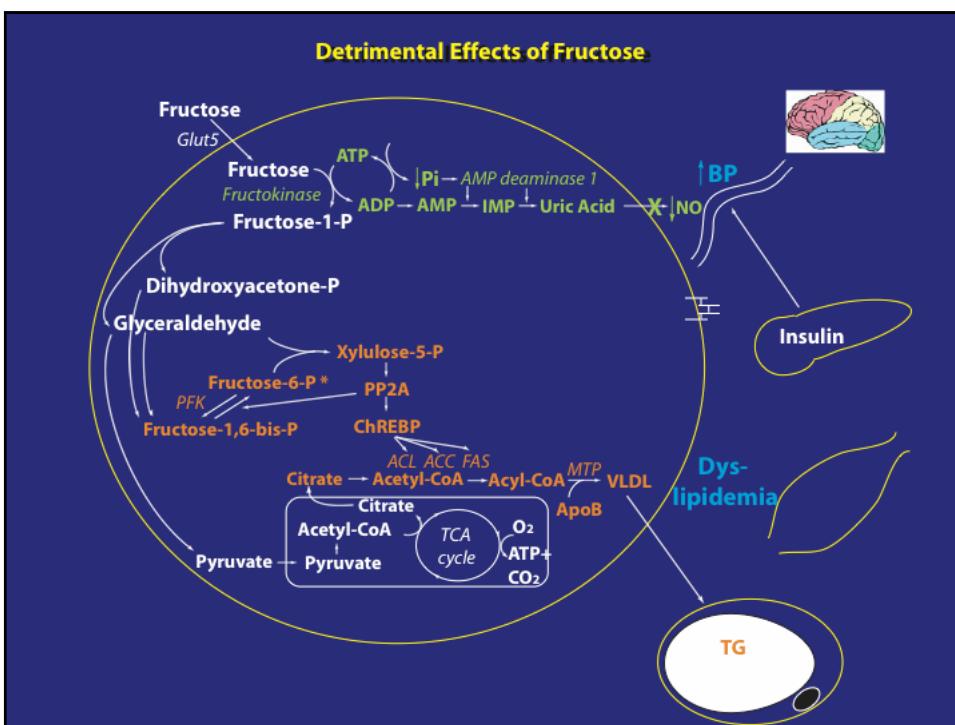
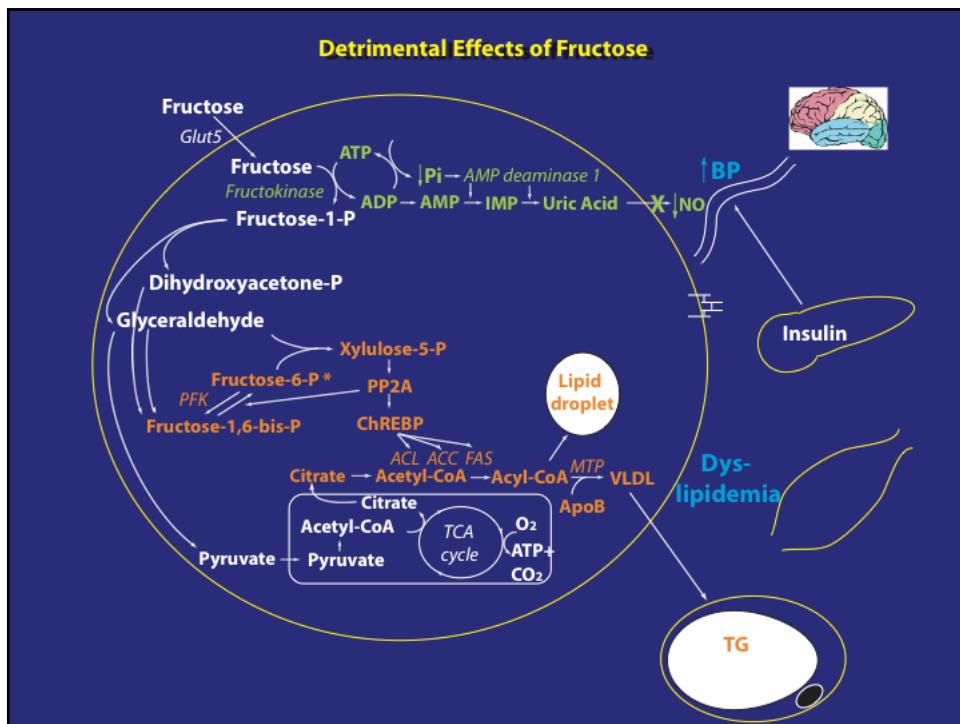


FIG. 7. NEFAs expressed as absolute values (A) and in percentage of the baseline value (B) during enoxaparin-induced lipolysis after control condition (○), after 28 days of fish oil supplementation (▨), after 6 days of high-fructose diet (■), and after fish oil supplementation plus high-fructose diet (▨) in seven men. Values are means \pm SE represented by vertical bars. * $P < 0.05$ high-fructose diet versus control.

Faeh and Schwarz, Diabetes 54:1907, 2005





Relation between ALT and liquid calorie consumption

UCSF WATCH Clinic

210 observations

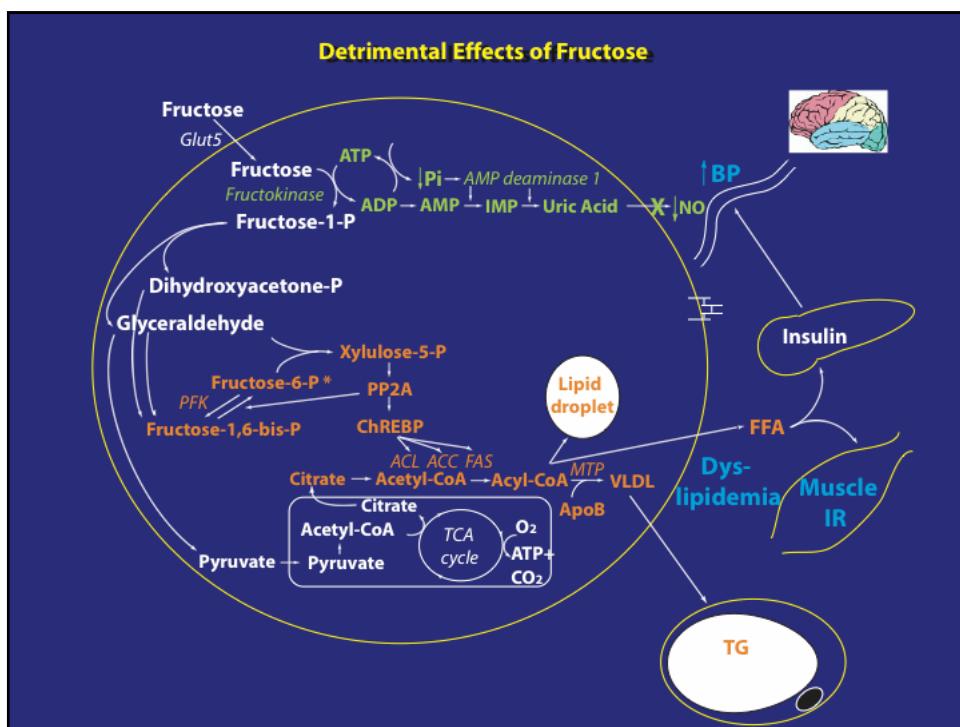
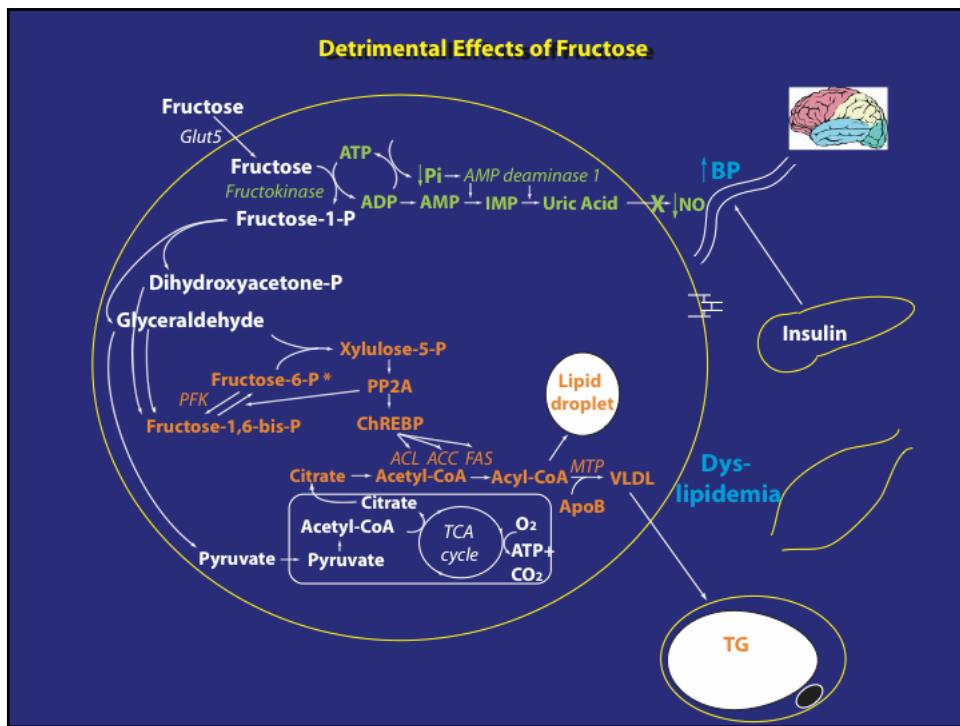
Univariate regression:

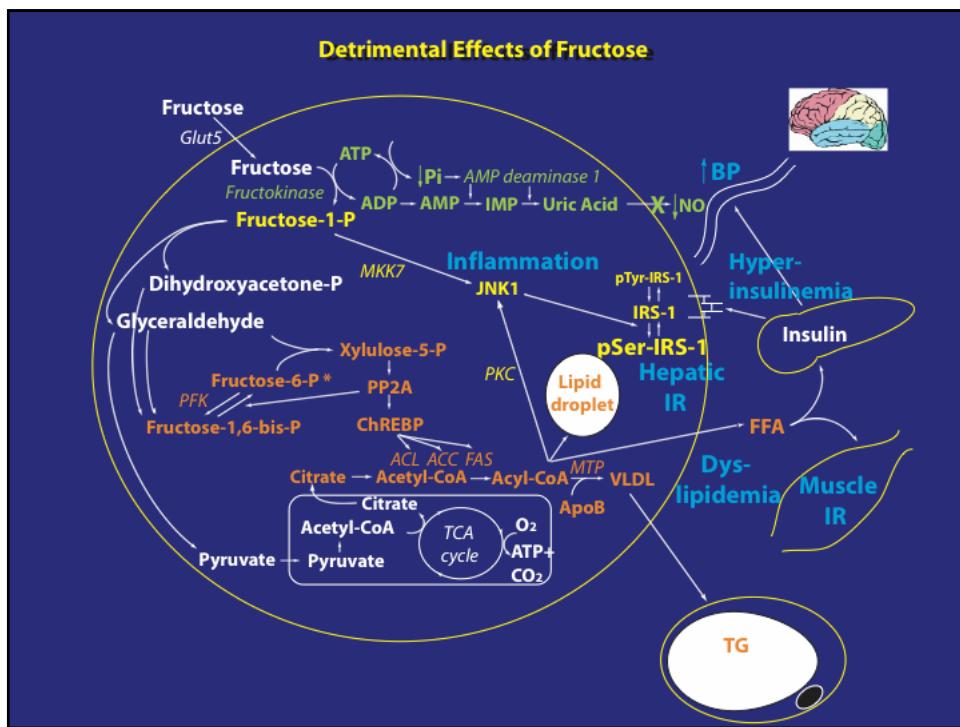
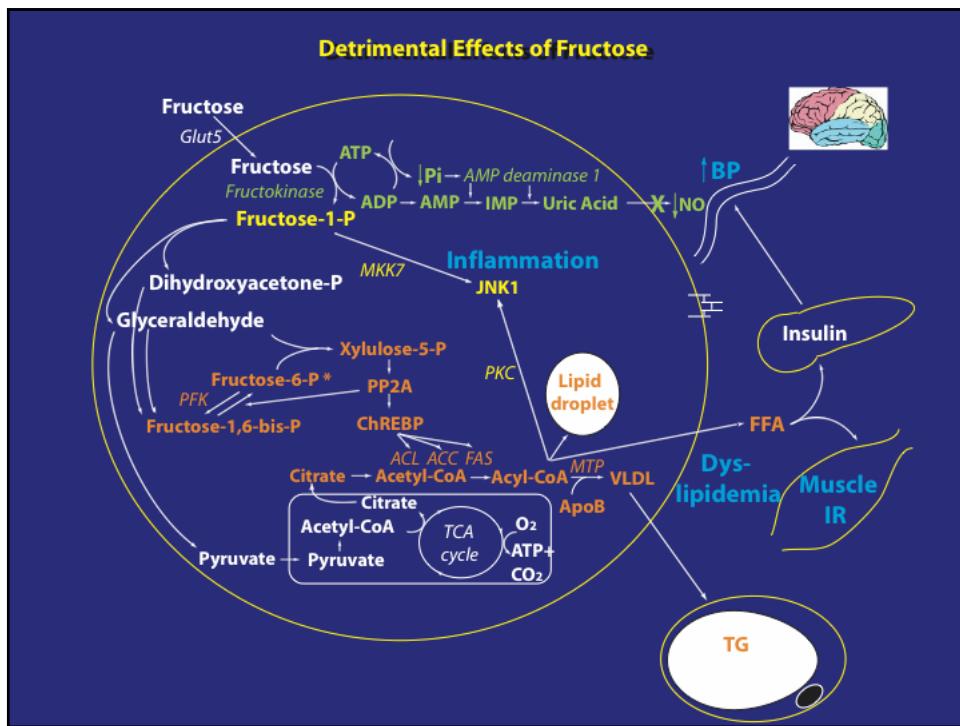
- Every 120 kcal/d increases ALT by 1 point ($p = 0.013$)

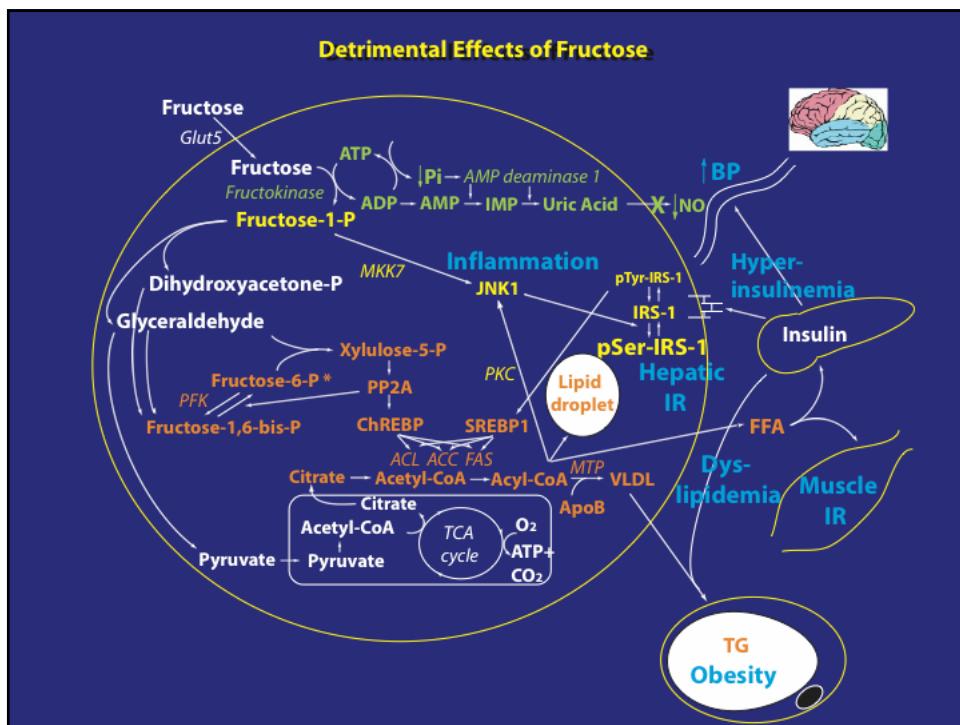
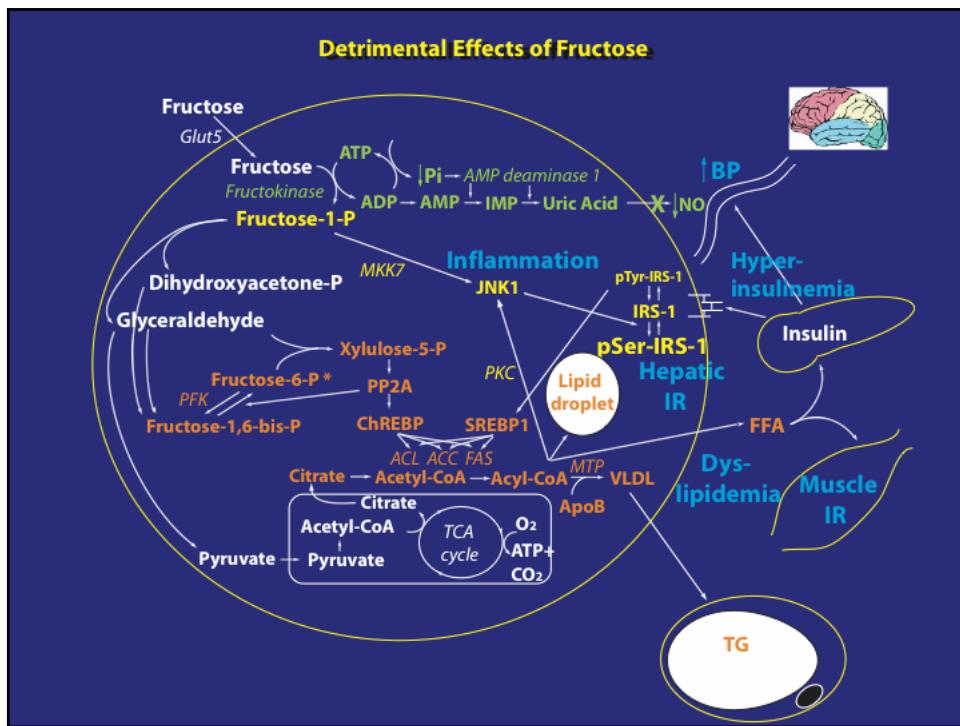
Multivariate regression:

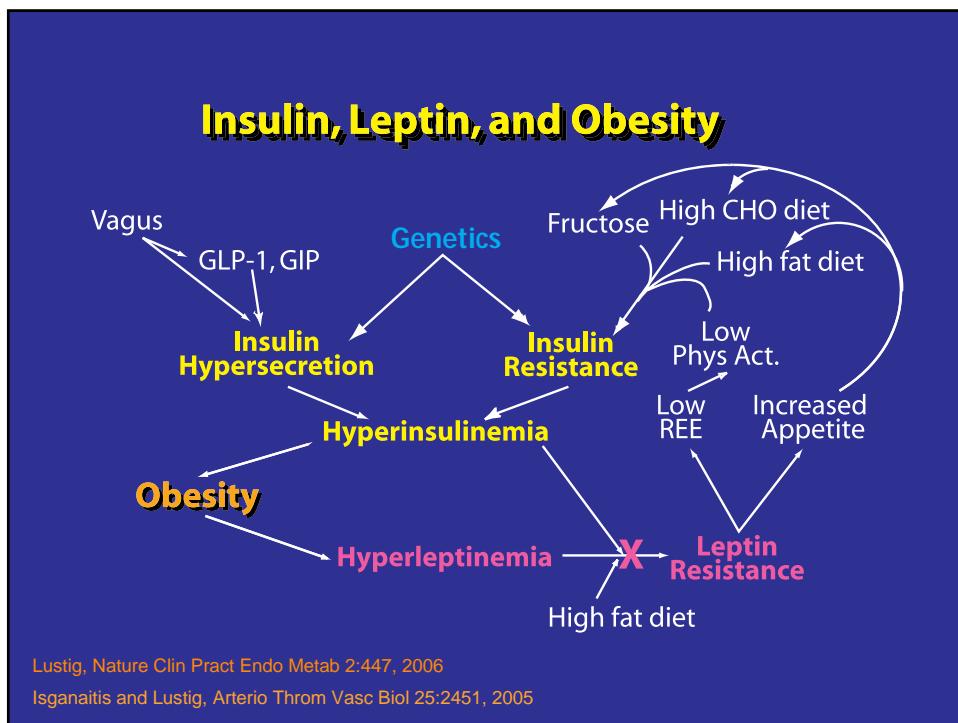
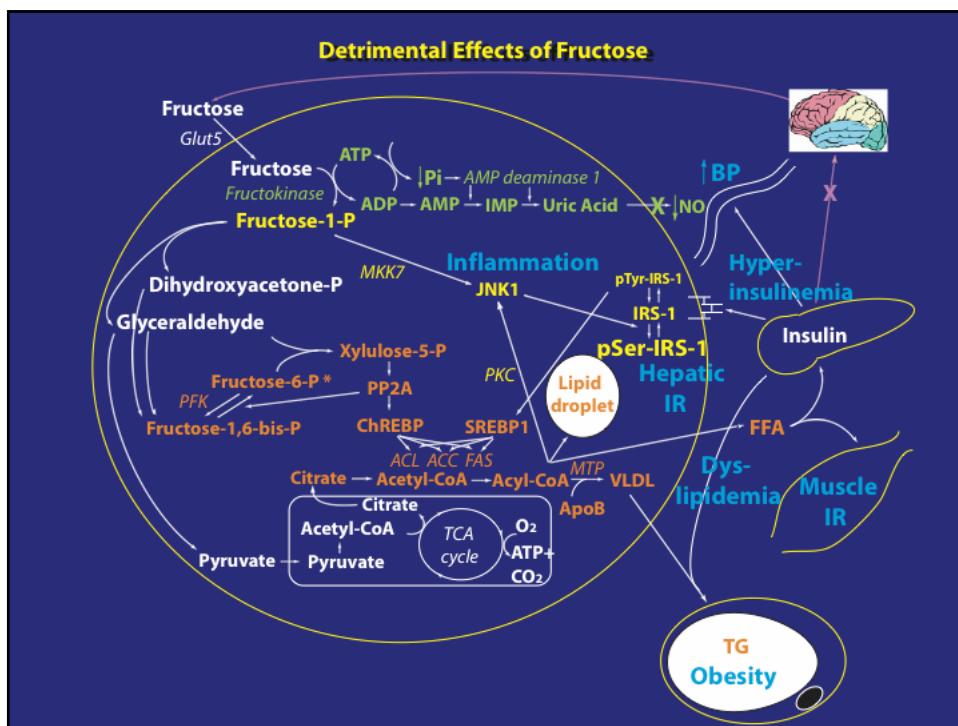
- HOMA-IR (insulin resistance) predicts ALT ($p = 0.048$)
- liquid calories correlates with ALT less well ($p = 0.1$)

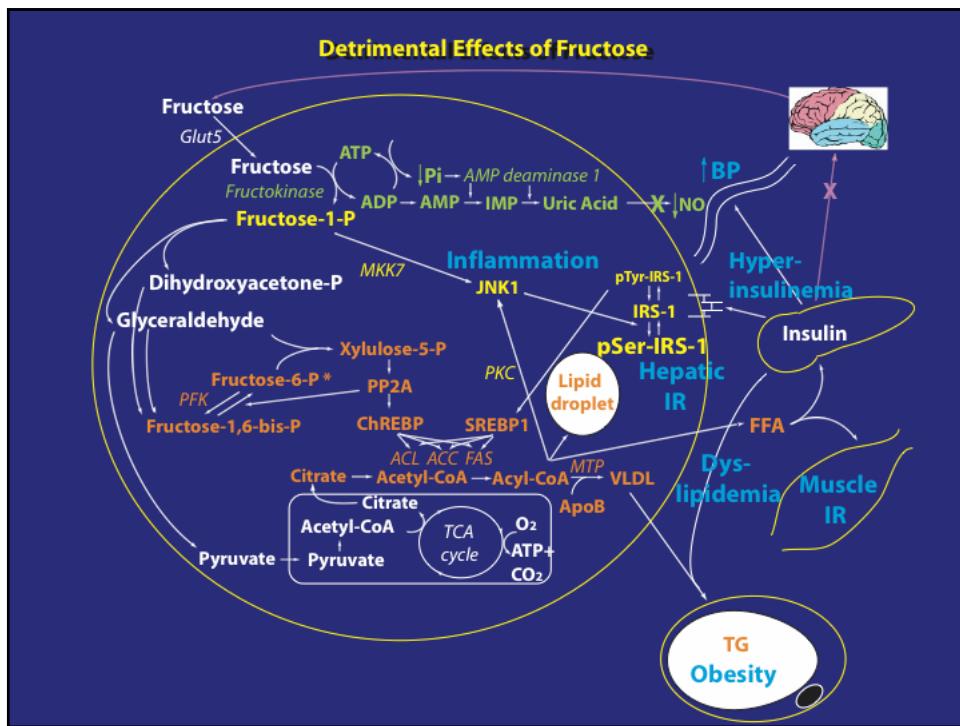
Mietus-Snyder et al. (in preparation)











Chronic ethanol exposure

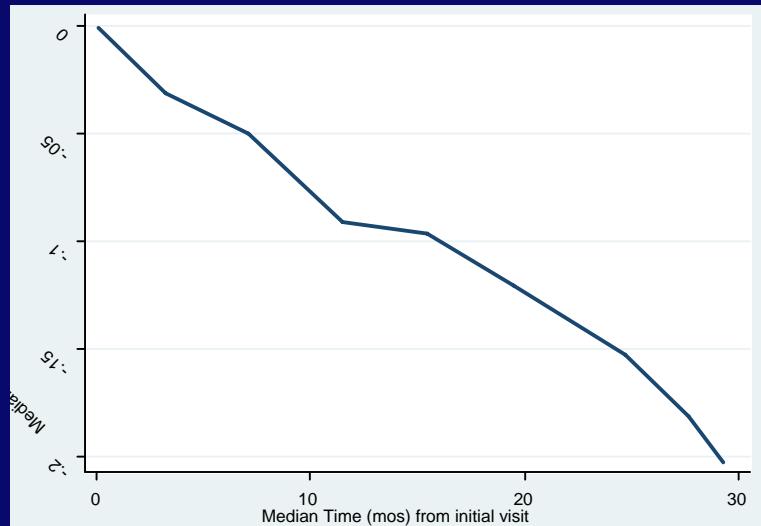
- Hematologic disorders
- Electrolyte abnormalities
- Hypertension
- Cardiac dilatation
- Cardiomyopathy
- Dyslipidemia
- Pancreatitis
- Malnutrition
- Obesity
- Hepatic dysfunction (ASH)
- Fetal alcohol syndrome
- Addiction

Chronic ethanol exposure	Chronic fructose exposure
• Hematologic disorders	
• Electrolyte abnormalities	
• Hypertension	• Hypertension
• Cardiac dilatation	
• Cardiomyopathy	• Myocardial infarction
• Dyslipidemia	• Dyslipidemia
• Pancreatitis	• Pancreatitis (2 ^o dyslipidemia)
• Malnutrition	
• Obesity	• Obesity
• Hepatic dysfunction (ASH)	• Hepatic dysfunction (NASH)
• Fetal alcohol syndrome	• Fetal insulin resistance
• Addiction	• Habituation, if not addiction

UCSF WATCH Clinic Associations with the Metabolic Syndrome			
Baseline Characteristic (mean ± SD)	HOMA-IR>5* N=124	HOMA-IR≤5 N=147	P-value**
BMI z-score	2.6, 2.3-2.8	2.5, 2.2-2.7	0.06
BP syst	125 ± 13	113 ± 15	<0.001
BP diast	68 ± 9	64 ± 8	<0.001
Triglyceride (mU/dl)	102, 69-138	83, 57-110	0.005
HDL-c (mU/dl)	41 ± 10	43 ± 10	0.04
Fasting Glc (mg/dl)	92 ± 9	85 ± 9	<0.001
Fasting Insulin (mU/ml)	33.7, 28.6-47.1	15.2, 11.2-19.8	<0.001
Creatinine (mg/dl)	0.64 ± 0.14	0.58 ± 0.15	0.003
ALT (U/L)	35, 23-50	23, 18-31	<0.001
MetS+	52%	29%	<0.001
Sugared Beverage Intake (kcal/d)	269, 100-423	129, 21-288	0.002
Breakfast (days/wk)	4, 0-7	7, 5-7	<0.001

Mietus-Snyder et al. (submitted)

UCSF WATCH Clinic Lifestyle Intervention: Median Change in BMI z-score from Baseline



Madsen et al. (submitted)

UCSF WATCH Clinic Predictors of Lifestyle Intervention

- Forward selection model, 4 variables

Source	SS	df	MS	Number of obs	= 130
Model	.169200646	4	.042300161	F(4, 125)	= 6.49
Residual	.81467663	125	.006517413	Prob > F	= 0.0001
Total	.983877276	129	.007626956	R-squared	= 0.1720
				Adj R-squared	= 0.1455
				Root MSE	= .08073

Delta z/yr	Coef.	Std. Err.	t	P> t	Beta
sugared_bev	.012786	.0048643	2.63	0.010	.2268616
HOMA	.0034239	.0018131	1.89	0.061	.1707474
Baseline_BMIZ	.0311507	.0199972	1.56	0.122	.1430862
Baseline_Age	.0027542	.0022543	1.22	0.224	.1055135
_cons	-.1475346	.0573037	-2.57	0.011	.

Madsen et al. (submitted)

Fructose is a carbohydrate

Fructose is a carbohydrate

Fructose is metabolized like fat

Fructose is a carbohydrate

Fructose is metabolized like fat

Fructose is also a toxin

Summary

- Fructose (sucrose vs. HFCS) consumption has increased in the past 30 years, coinciding with the obesity epidemic
- Fructose is everywhere
- Fructose is not glucose
- Hepatic fructose metabolism leads to all the manifestations of the **Metabolic Syndrome**:
 - hypertension
 - de novo lipogenesis, dyslipidemia, and hepatic steatosis
 - inflammation
 - hepatic insulin resistance
 - obesity
 - CNS leptin resistance, promoting continuous consumption
- Fructose ingestion interferes with obesity intervention
- Fructose is a chronic toxin

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